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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/534,091	05/06/2005	Juha-Matti Savola	TUR-168	2654

32954 7590 10/30/2008

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EXAMINER	
GEMBEH, SHIRLEY V	
ART UNIT	PAPER NUMBER
1618	
MAIL DATE	DELIVERY MODE
10/30/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/534,091	SAVOLA ET AL.	
	Examiner	Art Unit	
	SHIRLEY V. GEMBEH	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 August 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The response filed **8/12/08** presents remarks and arguments to the office action mailed **5/12/08**. Applicant's request for reconsideration of the rejection of claims in the last office action has been considered.

Applicant's arguments have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of Claims

Claims 23-32 are pending and examined in this office action.

Withdrawn Claim Objections

Examiner has withdrawn the allowability of claim 30 after careful consideration.

Claim 30 objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims is withdrawn.

Maintained Claim Rejections - 35 USC § 103 (clarification of the rejection is made below, no new reference is used)

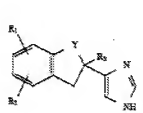
The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

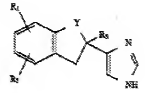
This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 23-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Karjalainen et al. US 5,498,623 in view of Geerts et al et al. US 5,658,938 and further in view of Chauveaux et al. US 6,326,401 and Huupponen et al. Clinical Pharmacol. Ther 1995; 58:506-511 (applicants prior art submission) (all of record) and Smith et al., US 2004/0236108 (of record).

Karjalainen et al. teach a compound as in current claim

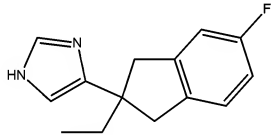


23 which is identical to that of the claimed compound of the

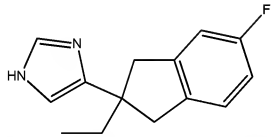


instant invention , wherein Y is CH_2 or CO, R_1 is a halogen or hydroxyl, $R_{2\,is}$ hydrogen or halogen and $R_{3\,is}$ hydrogen or lower alkyl-methyl (see abstract in a pharmaceutical composition administered orally (see abstract and also see col. 4, lines 62-63).

With regards to claims 24 and 25 the reference teaches (see abstract



also) 4-(2-ethyl-5-fluoro-2,3-dihydro 1H indan-2-yl)-1H-imidazole is the same as



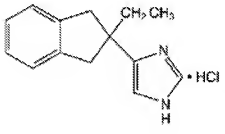
4-(2-ethyl-5-fluoro- indan-2-yl)-1H-imidazole or its salts. As to the hydrochloride salt of the said formula the reference teaches the preparation of such salt (see col. 7, lines 48-50).

Karjalainen et al. teach that the invention may be solid and the choice of auxiliary ingredients such as solvents and coloring are used in a normal way of the formulation as required by instant claim 26. See col. 6, lines 1-4.

The reference fails to teach the specific solvent, additives and or antimicrobial agents as required by the instant claims nor does it teach the spray formulation. Geertz, Chauveaux et al. and Smith et al. are applied for the teachings of an antimicrobial, flavoring and a solvent.

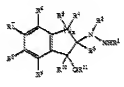
The Geerts et al. teach an imidazole compound (see abstract) wherein the composition comprises flavoring-thus interpreted as sweetening agents as in the instant claim 26 and the solvent is water (see col. 11, lines 16-20) as in claims 26-26 and 27. Known flavoring agents are lactose, aspartame glucose etc.

Chauveaux et al. teach antipamezole hydrochloride (see abstract) a drug that is within the core structure of the claimed compound



, wherein the solvent is water and alcohol-thus mixture thereof is within the claim limitation (see page 506, sec methods under heading and also page 507, under drug administration) in a form of spray (wherein one to four shots were given from bottles with atomizer designed to deliver…) (see lines 8-10 under drug administration, pg 507) as in claims 19-20 and 31-32. The reference also teaches the drug is oromucosal (see pg, 506, rt. col. four lines from the bottom). Chauveaux et al. teach that methyl and propyl parahydroxybenzoate is used as an antimicrobial agent in an oramucosal formulation (see col. 3, lines 36-45) as required by instant claims 26, 28 claim 30 in part, 31 and 32.

Huupponen et al. teach the pharmacokinetics of buccal mucosa administration of atipramezole in humans, that the absorption via oral mucosa is uniformal and the reference clearly teaches that absorption of antipamezole (same compound as Chaveaux) showed high bioavailability when administered oramucosally.

Smith et al. teach administering a core structure that is similar to the instantly claimed compound  see abstract. The compound is administered oromucosally see para 0079.

Smith teaches also that these classes of compounds are administered oromucosally.

One of ordinary skill in the art would have been motivated to modify the compounds taught by Karjalainen et al. and formulate an oromucosal formulation of the above formulation with the inclusion of a preservative because the Chauveaux et al. teach the composition of similar compound have been formulated with a preservative. The addition of the preservative is for preserving the homogenous formulation as taught in col. 3, lines 39-42 of Chaveaux et al. Thus one of ordinary skill in the art would have been motivated to incorporate a preservative in the formulation.

Even though the combined cited references do not teach a particular favoring to the composition, one of ordinary skill in the art would have been motivated to add flavorings to the composition/formulations for the improvement of taste. It is within the purview of the skilled artisan to add different flavors such as black currant because it does not only give flavor it also adds color that is appealing particularly to kids. The addition of different flavors is a result of the intended patient population. This is not

new and is a common practice in kid's medication such as Tylenol which comes in various flavors. Thus, one of ordinary skill in the art would be motivated to use a flavor that will give both taste and color to the drug that is used for oromucosal administration. Chaveaux et al further teaches that oromucosal administration is advantageous because it is the fastest possible medicamentous effect wherein degradation of the active substance is not in the gastrointestinal tract. Therefore, one of ordinary skill in the art would have been motivated to combine the teachings of Chaveaux with Karjalainen et al. and Huupponen et al. and formulate an oromucosal composition that is via oral route because it is known in the art that oral mucosa administration yields higher bioavailability.

Thus, the claimed invention was prima facie obvious to make and use at the time it was made.

Applicant argues: that oromucosal administration results in significantly greater bioavailability, that the cited prior art fails to show prima facie case of obviousness. That Karjalainen et al., Geertz et al. fail to teach oromucosal administration., and that Huupponen teaches the core structure but do not contain a halogen or hydroxyl at R1.

Examiner's Response: Karjalainen et al. teaches the instantly claimed compounds, yes it fails to teach oral mucosal, however, the additional references teaches that compounds with core structures have been used oromucosally in the prior art. Examiner, correctly added references that makes it obvious to one of ordinary skill in the art to employ the prior art teachings and arrive at the instantly claim invention.

The test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). As clearly depicted above the references applied would have rendered the instantly claimed method of administration obvious to one of ordinary skill in the art. Huuponnen makes it clear that oramucosal administration yields higher bioavailability. The compounds are all structurally related and having a different R-moiety would not play a role here because it is known in the art, that these compounds are administered oramucosally and has been taught to have high bioavailability.

Applicant's arguments have been fully considered but they are not persuasive. See above reasoning's.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHIRLEY V. GEMBEH whose telephone number is (571)272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, MICHAEL HARTLEY can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618
/SVG/
10/23/08